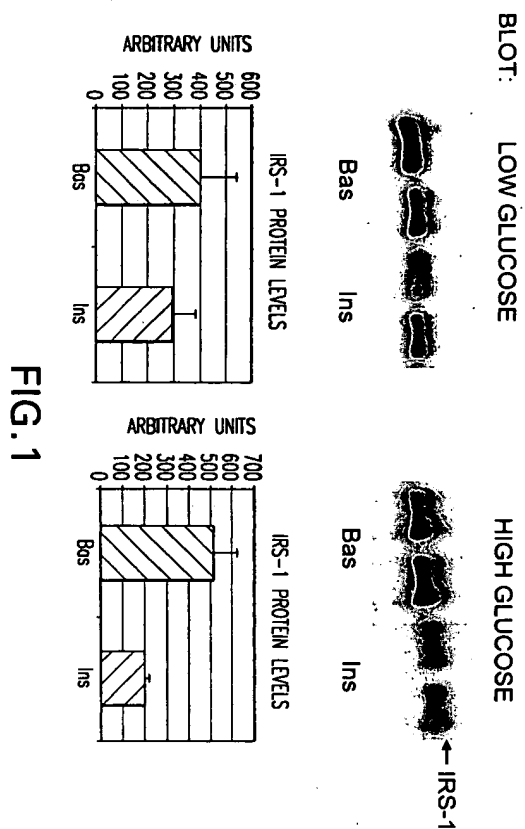


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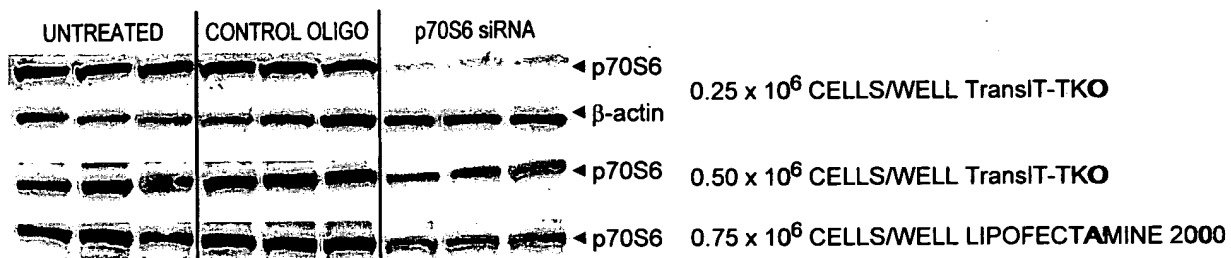


FIG.2

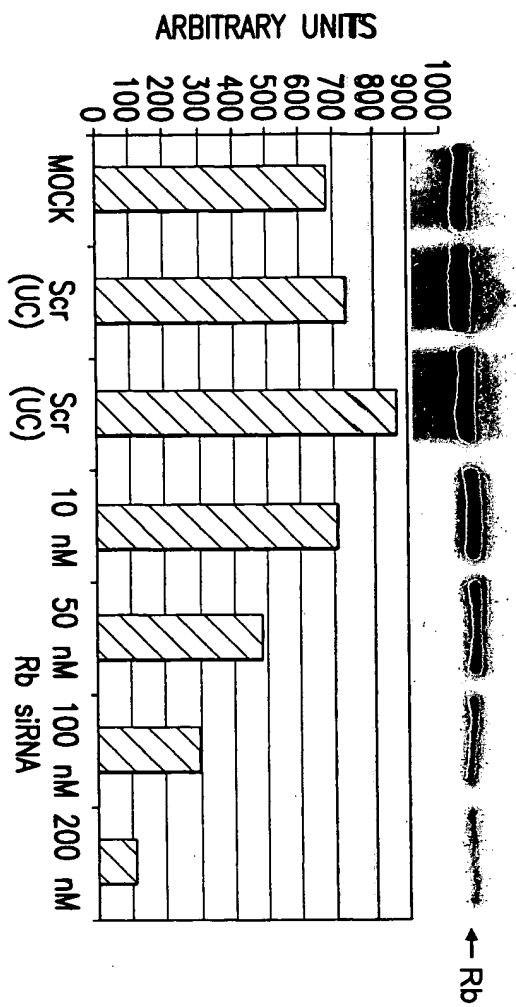
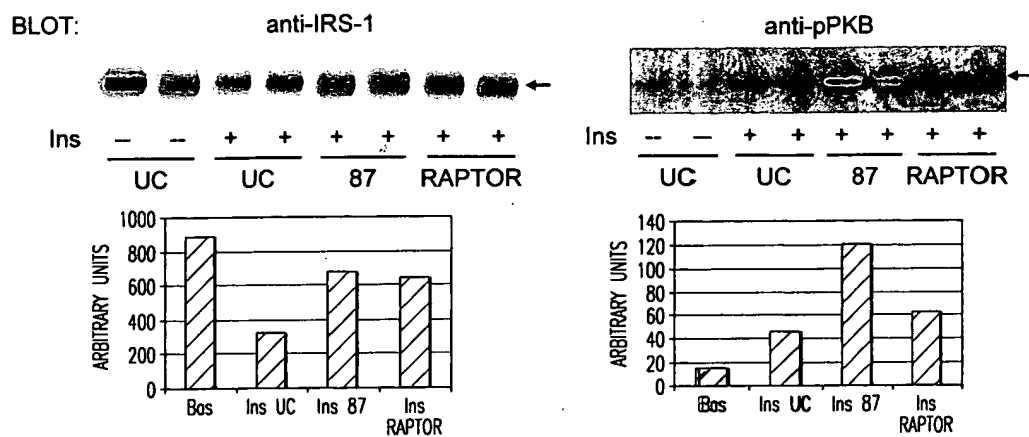


FIG.3



**FIG.4**

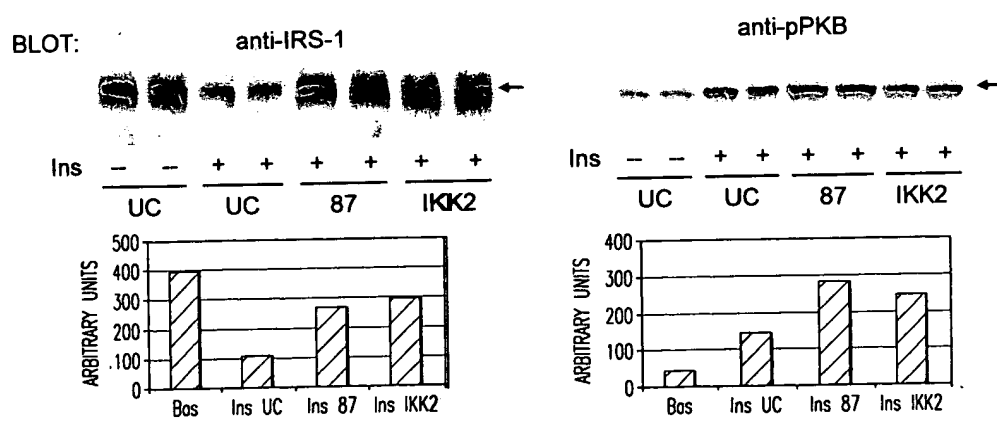


FIG.5

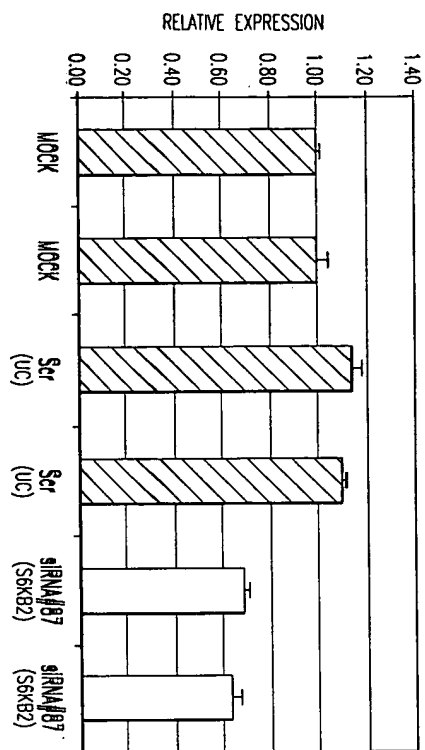
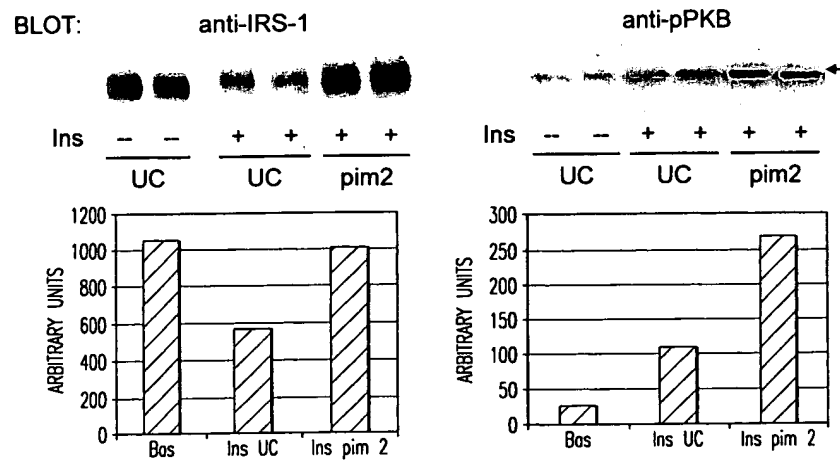


FIG. 6



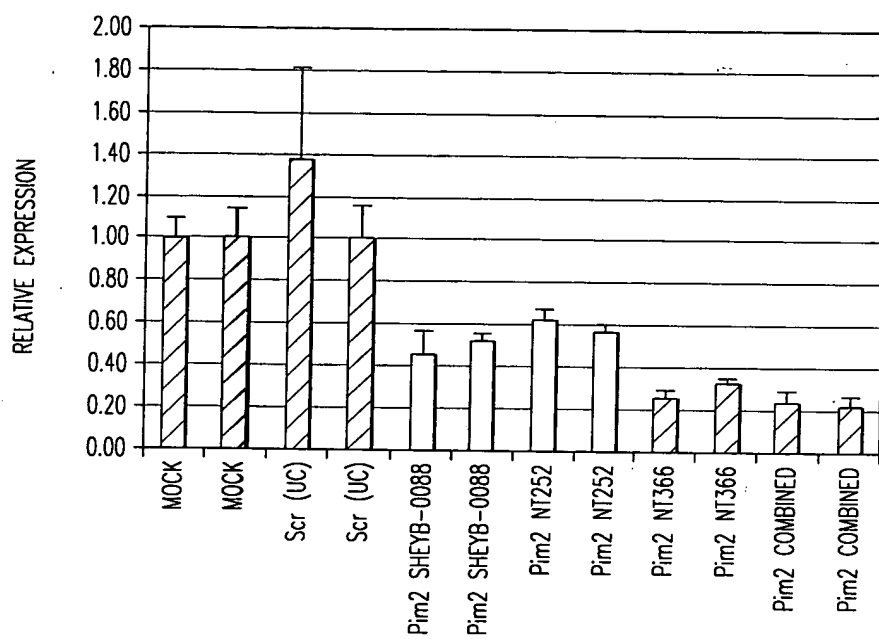
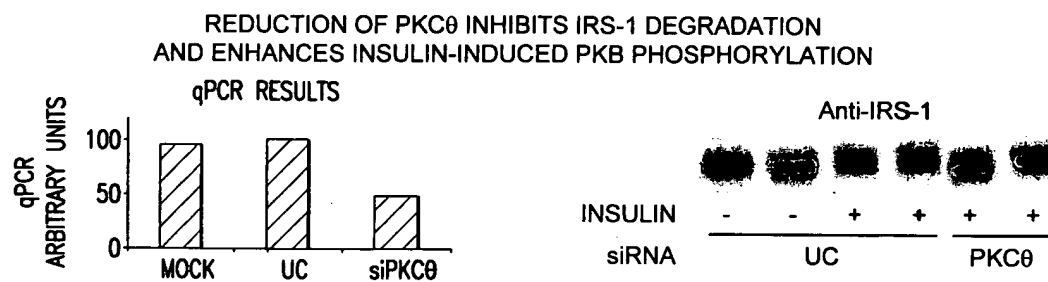
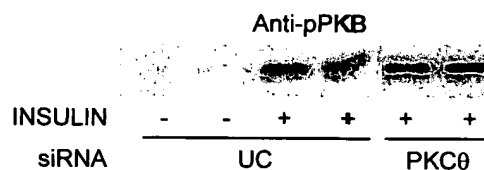


FIG.8



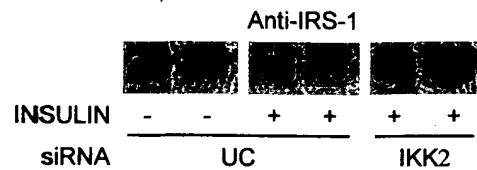
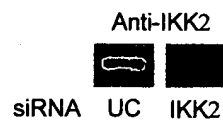


- FFA-INDUCED INSULIN RESISTANCE IS ASSOCIATED WITH ACTIVATION OF PKC $\theta$
- PKC $\theta$  KO MICE ARE PROTECTED FROM LIPID INDUCED INSULIN-RESISTANCE
- INCREASED PKC $\theta$  IN MUSCLE OF PATIENTS WITH TYPE 2 DIABETES
- CHRONIC HYPERINSULINEMIA INCREASES PKC $\theta$  EXPRESSION



**FIG.10**

REDUCTION OF IKK2 INHIBITS IRS-1 DEGRADATION AND  
ENHANCES INSULIN-INDUCED PKB PHOSPHORYLATION



- OVEREXPRESSION OF IKK2 CAUSE INSULIN RESISTANCE
- EXPRESSION OF DOMINANT NEGATIVE IKK2 REVERSES TNF, FFA AND HYPERGLYCEMIA INDUCED RESISTANCE
- IKK2 HAS BEEN SHOWN TO BE A TARGET OF HIGH DOSE SALICYLATES
- HETEROZYGOUS DELETION (*ikkbeta*<sup>+/-</sup>) PROTECTED AGAINST THE DEVELOPMENT OF INSULIN RESISTANCE DURING HIGH-FAT FEEDING AND IN OBESE (*ob/ob*) MICE

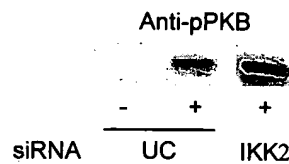
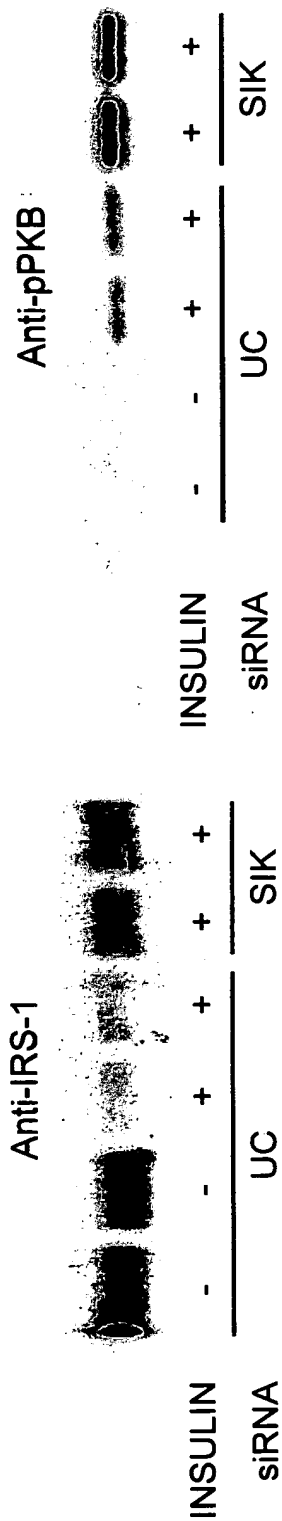


FIG.11

SALT-INDUCIBLE KINASE-1 (SIK) IS A NEW  
KINASE INVOLVED IN INSULIN RESISTANCE



- SIK was first cloned from the adrenal glands of rats fed a high salt diet
- Serine/threonine protein kinase that belongs to AMPK family
- SIK1 mRNA is elevated in adipose tissues, livers, and skeletal muscle of diabetic animals
- Involved in the phosphorylation of Ser789 in IRS-1 in livers of diabetic animals

FIG.12

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